

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Application of  
**BADORC, et al.**

Examiner: **RAHMANI, Niloofar**

Application No.: **10/509,919**

Art Unit: **1625**

Filed: **October 4, 2004**

Title: **NOVEL 1,2,3-SUBSTITUTED INDOLIZINE DERIVATIVES, INHIBITORS  
OF FGFS, METHOD FOR MAKING SAME AND PHARMACEUTICAL  
COMPOSITIONS CONTAINING SAME**

**RESPONSE TO RESTRICTION REQUIREMENT**

Commissioner for Patents  
P. O. Box 1450  
Alexandria, VA 22313-1450

Dear Sir:

This response is to the Examiner's Office Action, mailed March 28, 2007 (hereinafter, "Office Action").

Applicants file herewith a Petition for Extension of Time for one (1) month, or until May 29, 2007.

The Commissioner is hereby authorized to charge any additional fees that may be required for this filing, or credit any overpayment to Deposit Account Number 18-1982, upon which the undersigned is authorized to draw.

**Discussion and Traversal of the Restriction Requirement**

The Examiner has required restriction under 35 U.S.C. 121 and 372, alleging that the "application contains...inventions or groups of inventions, which are not so linked as to form a single general inventive concept under PCT Rule 13.1." (Office Action at 2).

The Examiner has required election of the invention of one of the Examiner's Groups I to IV:

- I. Claims 1-5, and 13-14, drawn to a compound of formula (I), wherein A being -CO-...;
- II. Claims 1-5, and 13-14, drawn to a compound of formula (I), wherein A being -SO-...;
- III. Claims 1-5, and 13-14, drawn to a compound of formula (I), wherein A being -SO<sub>2</sub>-...; and
- IV. Claims 15-30, drawn to a method for the treatment of disease requiring modulation of b-FGFs...

The Examiner has also required election of a single disclosed species within the elected Group.

Notwithstanding the Examiner's assertions, Applicants respectfully traverse this restriction requirement.

Citing PCT Rule 13.2, the Examiner acknowledges that "the requirement of unity of invention...shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features." (Office Action at 3). The Examiner further acknowledges that Annex B, Part 1(a) indicates that, "the application should relate to only one invention, or if there is more than one invention, inclusion is permitted if they are so linked to form a single general inventive concept." (Office Action at 3, emphasis added).

Accordingly, even though the inventions of the Examiner's groups I to IV may be patentably distinct inventions, they may still be examined together where they are so linked as to form a single general inventive concept.

As in the present case, which involves in particular Markush Practice, Annex B Part 1(f) indicates that, “wherein a single claim defines alternatives...the requirement of a technical interrelationship...shall be considered to be met when the alternatives are of a similar nature.” Part 1(f) then goes on to provide,

When the Markush grouping is for alternatives of chemical compounds, they shall be regarded as being of a similar nature where the following criteria are fulfilled: (A) all alternatives have a common property or activity, and (B)(1) a common structure is present, i.e., a significant structural element is shared by all of the alternatives... ((A) and (B)(1) are also quoted by the Examiner. (Office Action at 3)).

Further citing Part 1(f), the Examiner acknowledges that, “the common structure must...occupy a large portion of their structure, or...the common structure constitutes a structurally distinctive portion.” (Office Action at 4).

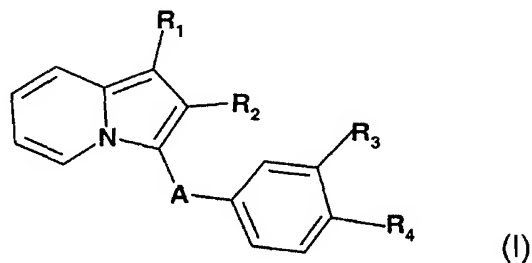
As discussed in detail below, the compounds of the present application do, indeed, have a common structure that occupies a large portion of their structure and the common structure does, indeed, constitute a structurally distinctive portion.

As the Examiner indicates, citing part 1(f)(v), “When dealing with alternatives, if it can be shown that at least one Markush alternative is not novel over the prior art, the question of unity of invention shall be reconsidered by the Examiner.” (Office Action at 4).

The Examiner then alleges that, “In the instant case, at least one Markush alternative is not novel because prior art by Zhang et al., Synthesis, ‘A One-step Approach to 1-(fluoroalkyl) indolizine Derivatives’, 1999, Vol. 1, pages 51-54 [hereinafter “Zhang”] anticipated group I, thus the lacking of unity of invention has been found.” (Office Action at 4).

As discussed in detail below, and notwithstanding the Examiner’s allegations, Zhang does not anticipate any compound of the present invention.

All of the compounds of the present invention are encompassed by formula (I),

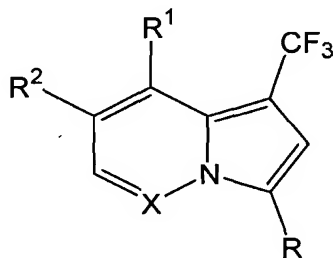


The Examiner has restricted around the value of the linking group, A, which represents the small linking groups  $\text{-CO-}$ ,  $\text{-SO-}$  or  $\text{-SO}_2\text{-}$ . Thus, the substituted indolizine ring, and the substituted phenyl ring are common to all compounds of the present invention.

Accordingly, “all alternatives have a common property or activity...and a common structure is present, i.e., a significant structural element is shared by all of the alternatives” and “the common structure [occupies] a large portion of their structure”, and “the common structure constitutes a structurally distinctive portion.” Thus, all of the requirements provided for in Annex B are met by the Markush group of the present invention.

The Examiner asserts that Zhang anticipates the Examiner’s group I. (Office Action at 4). Notwithstanding the Examiner’s assertion, this is not the case.

The compounds of Zhang which come closest to the compounds of the present invention are given by the formula found at page 51 of Zhang, i.e.,



The compound wherein R<sup>1</sup> and R<sup>2</sup> of Zhang are both hydrogen, X of Zhang is CH, and R of Zhang is CPh is that of 3aa of Zhang, found in the Table on page 52. This compound is, indeed, a benzoyl indolizine, and the one closest to the compounds of the present application. However, this compound has a -CF<sub>3</sub> moiety at the 1-position of the indolizine. This position corresponds to R<sub>1</sub> of formula I of the present application.

The -CF<sub>3</sub> moiety is not a possible value for R<sub>1</sub> as defined by the claims of the present application.

Other compounds of Zhang either require substitution in the phenyl portion of the indolizine ring, which is not found in the compounds of the present application, or are not substituted by the benzoyl moiety at the 3-position of the indolizine ring, as required by the compounds of the present invention.

Therefore, Zhang does not anticipate either the Examiner's Group I, or any other of the Examiner's Groups.

Accordingly, the Unity of Invention requirements of Annex B are met, and there is no anticipation of any group by the prior art cited by the Examiner.

In view of this, Applicants respectfully request reconsideration and withdrawal of the restriction requirement.

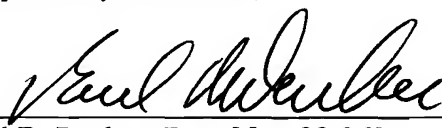
#### Election

In order to comply with the requirements of 37 C.F.R. § 1.143, Applicants provisionally elect, with traverse, and should the Examiner's Restriction Requirement be made final, the invention of Examiner's Group I, i.e., claims 1 to 5, and claims 13 and 14, wherein A is -CO-.

As required by the Examiner, Applicants further elect, with traverse, the species disclosed in the specification, for example, at page 83, in Table IX, as Example 150, i.e., 2-amino-5-[(1-methoxy-2-methyl-3-indoliziny)carbonyl]benzoic acid.

Respectfully submitted,

Dated: May 23, 2007

  
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